

Application No. 10/688,786  
Reply to Office Action of February 1, 2005

### REMARKS

With this response, Claims 1-40 are pending in the application. Claims 36-40 have been withdrawn from consideration, and Claim 11 has been amended.

#### Non Art-Based Rejections

##### Claim Objections

In the Office Action, Claim 11 was objected to because of the presence of "ins." With this response, "ins" has been corrected to "is." Withdrawal of the objection is respectfully requested.

Claim 30 currently stands objected to as depending from a rejected base claim. Applicants acknowledge the Examiner's determination that Claim 30 would be allowable if re-written in independent form. For the reasons given below, however, Applicants submit that the base claim for Claim 30 is allowable and so decline the Examiner's invitation to re-write Claim 30 as an independent claim at this time.

#### Art-Based Rejections

##### Rejections Under 35 U.S.C. 102

Applicants acknowledge that no claims stand rejected under 35 U.S.C. 102.

##### Rejections Under 35 U.S.C. 103

In the Office Action, Claims 1, 2, 5-17 and 19-22 were rejected under 35 U.S.C. 103(a) as unpatentable over Bernstein et al. (U.S. Patent 6,749,866) in view of Lee and Timasheff, *J. Biol. Chem.*, 256(14):7193-7201 (1981). Applicants respectfully traverse these rejections.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the

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knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. See M.P.E.P. §§2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaack*, 947 F.2d 488 (Fed. Cir. 1991). Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed inventions, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "The factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Sang Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations and quotes omitted). Additionally, it is now well-established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability and [can] not be resolved on subjective belief and unknown authority." *In re Sang Su Lee*, 277 F.3d at 1343-44.

Applicants submit that the Patent Office has failed to present a *prima facie* case of obviousness. In the Office Action, it is admitted that Bernstein *et al.* do not disclose the use of a sugar in a sustained release composition. In the Office Action, it is alleged that Lee and Timasheff disclose that sucrose is preferentially excluded from the protein domain, thereby increasing the apparent activation energy of unfolding and thus stabilizing the protein. The Office Action then concludes that one would have been motivated to combine the references to obtain the present invention. Whatever else Lee and Timasheff teach, they do not teach the use of sucrose in a composition for sustained release of a biologically active peptide. Moreover, the Office Action does not point to anything in Lee and Timasheff to provide an expectation of success in a sustained release situation or in other than the sucrose water solvent system described in the reference. Applicants wish to point out that a determination of obviousness cannot be based on what a person of skill in the art might try. Rather, the proper test requires a determination of what the prior art would have led the skilled person to do. *In re Dow Chemical*, 837 F.2d

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469, 473 (Fed. Cir. 1988). Thus, the fact that a reference may pique a scientist's curiosity and that further research may be done as a result of the reference is insufficient to support a rejection under section 103 absent sufficient teaching in the reference of how to obtain the desired result or that the claimed result would be obtained if certain directions were pursued. *In re Lilly & Co.*, 9023 F.2d 943 (Fed. Cir. 1990). MPEP 2143.01 specifically provides that in establishing a *prima facie* case of obviousness, "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination."

Applicant's respectfully submit that light of the Patent Office's failure to identify any suggestion to combine within the cited references themselves, the Patent Office's reconstruction of the references in an attempt to obtain the presently claimed inventions necessarily and inevitably requires the application of impermissible hindsight. In light of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 1, 2, 5-17 and 19-22 as obvious over *Berstein et al.* in view of Lee and Timasheff.

In the Office Action, Claims 3, 4, 18 and 31-35 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Berstein et al.* in view of Lee and Timasheff in further view of Taylor *et al.*, *Diabetes*, 51(Suppl. 2):85 (2002). Applicants respectfully traverse the rejection of these claims and submit that the Office Action fails to present a *prima facie* case under 35 U.S.C. 103(a).

The alleged teachings of *Berstein et al.* and Lee and Timasheff have been discussed in reference to the rejection of Claims 1, 2, 5-17 and 19-22. In the Office Action, Taylor *et al.* is alleged to teach infusion of synthetic exendin-4 to type 2 diabetics over 10 days. Arguments made by applicants regarding the legal requirements to sustain a 103 rejection made in conjunction with the rejection of Claims 1, 2, 5-17 and 19-22 apply with equal force to the instant rejections and are incorporated herein. Applicants again submit that the Office Action has failed to point to any objective evidence of a motivation to combine or reasonable expectation of success within the cited references themselves. In particular, applicants note that the Office Action does not identify any teaching suggestion in Taylor *et al.* regarding sustained release compositions. Instead the

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Office Action relies on conclusory statements regarding the teachings of the combined references; something the Federal Circuit has repeatedly stated the Patent Office cannot do in the context of a 103 rejection. At least for these reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 3, 4, 18, and 31-35 under 35 U.S.C. 103(a) as being unpatentable over Bernstein in view of Lee and Timasheff and further in view of Taylor *et al.*

Claims 23-29 presently stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bernstein *et al.*, in view of Lee and Timasheff, and in further view of Silvestri *et al.* (U.S. Patent No. 5,126,147). Applicants respectfully traverse the rejection of these claims and again submit that the Office Action fails to present a *prima facie* case of obviousness under section 103. The alleged teachings of Bernstein *et al.* and Lee and Timasheff have been discussed in reference to the rejection of Claims 1, 2, 5-17 and 19-22. In the Office Action, Silvestri *et al.* are alleged to teach a sustained delivery system comprising a bioactive agent, a bioerodible polymer, and a corticosteroid. The requirements necessary for the Patent Office to meet its burden of proof regarding a *prima facie* case of obviousness have been discussed above in the context of the rejection of Claims 1, 2, 5-17 and 19-22 and apply with equal force to rejection of the instant claims. Applicants again respectfully submit that the Office Action fails to point to objective evidence of record of a motivation to combine and a reasonable expectation of success, but instead simply recites the alleged teachings of the references and concludes that such motivation and expectation exist. What is not found in the Office Action is any objective evidence of record as to why the skilled artisan would have selected the particular components from these references and combined them in the manner of the claimed invention. Additionally the Office Action fails to even address the requirement for evidence of a reasonable expectation of success. Absent such evidence, the Patent Office has failed to meet its burden of proof. Applicants therefore, respectfully request reconsideration and withdrawal of the rejection of Claim 23-29 under 35 U.S.C. 103(a).

In the Office Action, Claims 1, 2, 5-17 and 19-22 were rejected under 35 U.S.C. 103(a) as unpatentable over Woiszwilllo *et al.* (U.S. Patent No. 5,981,719) in view of Bernstein *et al.* Applicants respectfully traverse the instant rejection of these claims. The

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alleged teachings of Bernstein *et al.* have been discussed in reference to the rejection of Claims 1, 2, 5-17 and 19-22. In the Office Action, Woiszwillo *et al.* are alleged to disclose a sustained release composition comprising microparticles formed by mixing a macromolecule with a polymer and optionally a sugar. Again, Applicants respectfully submit that the Office Action fails to present a *prima facie* case of obviousness under 35 U.S.C. 103. Instead, the Office Action simply recites the alleged relevant teachings of references and concludes that one skilled in the art would be motivated to combine the references. Applicants again repeat the arguments regarding the legal standard for an obviousness rejection made in conjunction with the rejection of Claims 1, 2, 5-17 and 19-22 and point out that conclusory statement by the patent office cannot substitute for objective evidence of a motivation to combine. Additionally, the Office Action does not address the expectation of success. Applicants respectfully wish to point out that the standard is not either a motivation to combine or a reasonable expectation of success, but both. This failure of the Office Action to address the expectation of success is, by itself, sufficient to defeat a *prima facie* case of obviousness. At least for these reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 1, 2, 5-17 and 19-22 under 35 U.S.C. 103(a) over Woiszwillo *et al.* in view of Bernstein *et al.*

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**Information Disclosure Statement**

An Information Disclosure Statement is being filed concurrently herewith.

**Conclusion**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

ELMORE, CRAIG & VANSTONE, P.C.

By 

Carolyn S. Elmore

Registration No: 37,567

Telephone: (978) 251-3509

Facsimile: (978) 251-3973

N. Chelmsford, MA 01863

Dated: 